REMARKS

Allowable Subject Matter

Applicants gratefully acknowledge the Examiner's indication that claims 1-3, 6-31 and 33-44 are free of the prior art.

Amendments

New claim 45 is directed to the scope of claimed subject matter discussed in the text bridging pages 2-3 of the Office Action issued April 20, 2006. Claims 46-48 recite variable groups exemplified in the specific compounds described in the specification. Claims 49-57 are directed to further method aspects of the invention. See, e.g., page 36, lines 14-18 and claim 31.

Withdrawn Subject Matter and Claim Objections

At pages 2-3 of the Office Action, the Examiner argues that based on the species elected by applicants, a certain narrow scope of the claimed subject matter has been examined. Further, the Examiner has determined that this examined scope is allowable (see the statement on page 9 of the Office Action that claims 1-3, 6-31 and 33-44 are free of the prior art). However, the Examiner has decided not to examine any further part of the claimed subject matter. No justification is presented in the Office Action for failing to continue examination of the scope as to, for example, all of the claimed compounds in which M is phenyl, or in which M is phenyl and D is absent, or in which M is phenyl, D is absent, and W is pyrazolediyl. Such action is clearly improper and violates the procedure, as set forth in the MPEP, for examination following an election of species and for examination of Markush claims.

The instant application is the US national phase of PCT application No. PCT/EP2003/005898. Unity of invention for PCT applications falls under PCT Rule 13. Rule 13.1 states that the application shall relate to one invention or a group of inventions linked to form a single general inventive concept (the unity of invention requirement). Rule 13.2 states that when there are a group of inventions then, to satisfy the unity of invention requirement, the inventions must involve one or more corresponding special technical features.

The claims involved here are Markush claims. As discussed in Annex B of the Administrative Instructions Under the PCT, entitled "Unity of Invention," (see pages AI-58 to AI-60 of the MPEP), for Markush claims the requirements under Rule 13.2 for unity of invention are met when: (1) the alternatives in the Markush claim have a common property or activity, and (2) either (a) the compounds share a significant structural element, or (b) the compounds all belong to a recognized class of chemical compounds. See also MPEP §1850 (III)(B).

Further, the Annex states that merely because members of the Markush claim can be differently classified does not justify a finding of lack of unity of invention. See section (f)(iv) of Annex B.

It is evident that compounds of applicants' Markush group satisfy the requirements of Rule 13.2 beyond the scope examined by the Examiner. For example, when M is phenyl and D is absent, all of the compounds have a phenyl ring as a core structure with up to three substituents. Thus, examination should continue beyond the scope already examined.

The original Restriction Requirement divided the compound claims based on individual compounds. Thus, this was an election of species requirement. In accordance with MPEP §809.02(c), upon determination that the elected species is allowable, as in the case here, examination will be extended to other species. Thus, the Examiner's decision to arbitrarily stop examination after examining a narrow scope of the claim is contrary to the procedure set forth MPEP §809.02(c).

Furthermore, applicants respectfully submit US law, specifically 35 USC §121, does **not** permit restriction within a single claim (except in one specific circumstance described below) as clearly indicated by the court in *In re Weber et al.,* 198 USPQ 328 (1978).

> As a general proposition, an applicant has a right to have *each* claim examined on the merits. If an applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications. Such action would not affect the right of the applicant eventually to have each of the claims examined in the form he considers to best define his invention. If, however, a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits.
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> It is apparent that §121 provides the Commissioner with the authority to promulgate rules designed to *restrict* an *application* to one of several claimed inventions when those inventions are found to be

"independent and distinct." It does not, however, provide a basis for an examiner acting under the authority of the Commissioner to *reject* a particular claim on that same basis. [*Weber* at 331-332]

The effect of restriction within a single claim is the same as a rejection. 35 USC §121 does not give the Commissioner authority to require that a single claim "be divided up and presented in several applications" and thus deny the applicant the right to have that single claim considered on its merits. This is exactly the action that the Court in *Weber* stated was not permitted under 35 USC §121. Such action by an Examiner would violate "the basic right of the Applicant to claim his invention as he chooses." [*Weber* at 332]

As discussed in MPEP §803.02, '[s]ince the decisions in *In re Weber,* 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention." Thereafter, the MPEP cites *In re Harnish*, 206 USPQ 300 (CCPA 1980) and *Ex parte Hozumi*, 3 USPQ2d (Bd. Pat. App. & Int. 1984).

These two cases, *Harnish* and *Hozumi,* both deal with improper Markush rejections. Thus, in the case of Markush claims, refusal by the Office to examine that which the applicants regard as their invention, by restricting within a Markush claim, must be a refusal based on an improper Markush rejection. In both *Harnish* and *Hozumi*, the Court and the Board, respectively, decided that the Markush groups in question were **not improper,** and therefore restriction within a claim was not permitted. Thus, in the case of a proper Markush grouping, restriction within a claim is not permitted.

No improper Markush rejection has been with respect to applicants' Markush claims. Thus, examination should proceed in accordance with MPEP §803.02.

Applicants respectfully request the Examiner to extend the examination of the claimed invention beyond the scope set forth art page 2-3 of the Office Action.

Rejection under 35 USC § 112, first paragraph, enablement

Claims 27, 28, 31, and 33 are rejected under 35 USC § 112, first paragraph, on grounds of alleged lack of enablement. This rejection is respectfully traversed.

Firstly, it is gratefully noted that the Examiner has acknowledge that the claims are

enabling for the treatment of thomboembolic disorders. See the bottom of page 4 of the Office Action. See also, for example, applicants' claims 49, 50, and 58.

A disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must be taken as in compliance** with the enabling requirement of the first paragraph of section 112, unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995).

The courts have placed the burden upon the PTO to provide **evidence** shedding doubt on the disclosure as to whether the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). Furthermore, the court's comments in *Marzocchi* make it clear that examples are not required, and thus an assertion of a lack of specific examples does not, in and of itself, establish non-enablement.

> The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

The MPEP also agrees by stating that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

In the instant case, the Examiner argues that there is "no absolute predictability" in the art. This is not the test for enablement. Absolute predictability is not required under the statute. In addition, merely because an art is alleged to be unpredictable does not establish non-enablement. See, e.g., *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976) in which the art involved (catalysis) was acknowledged to be unpredictable, yet the court still found the disclosure in question to be enabling.

The Examiner argues that the Wong et al. article teaches a structurally similar compound as an inhibitor of factor Xa and further that Wong et al. disclose only a connection between factor Xa and myocardial infarction, unstable angina, deep vein thrombosis, pulmonary embolism, and ischemic stroke. However, there is nothing to suggest that the Wong et al. disclosure is intended to provide a complete comprehensive list of all conditions associated with factor Xa. The same is true for the Sampson et al. article. As for the

Schulman et al. article, this article clearly sates that their "findings strongly support the impression that warfarin has an antineoplastic effect" (page 1957).

The Examiner concludes that "in the absence of a showing of correlation" between the diseases recited in the claims and factors VII and Xa, one could not fully predict the possible results. However, it is the PTO's initial burden to present reasons to doubt, and the articles discussed in the rejection do not provide any reason to doubt the statements in applicants' specification regarding enablement. Further, as noted above, absolute predictability is not a requirement for enablement.

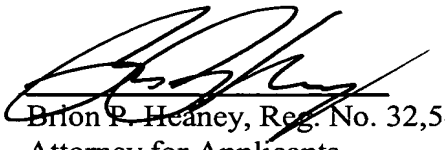
The rejection further argues that the antitumoral action of the compounds is not supported. Enclosed herewith is a copy of Fischer et al., "Tumor Cell Adhesion and Migration Supported by Interaction of a Receptor-protease Complex with its Inhibitor," J. Clin. Invest., November 1999, vol. 104, No. 9, pp1213-1221. This article clearly describes the antitumoral action of TF-VII inhibitors and also describes how to determine these activities. See also applicants' specification at pages 46-47 which present IC_{50} data demonstrating activity of compounds of the invention. The specification also provides detailed description of how to use the compounds of the invention as pharmaceutical agents. See, e.g., pages 35-37 and Examples A-H.

Moreover, contrary to the assertion in the rejection, it would not require undue experimentation to make and use the claimed invention. Determining the relative amount of activity a given compound requires no more than routine experimentation using the assays described in the specification and in the art. With regards to the amount of experimentation it is noted that even a considerable amount of experimentation, or complex experimentation, is permissible if it is routine. See, e.g., *Ex parte Jackson,* 217 USPQ 804, 807 (POBA 1982) and *In re Wands*, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988).

In view of the above remarks, it is respectfully submitted that applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with no more than routine experimentation. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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